Rhythm outcome predictors after concomitant surgical ablation for atrial fibrillation: A 9-year, single-center experience

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Objectives: Concomitant surgical ablation is a safe and feasible procedure, recommended by the guidelines for patients with atrial fibrillation (AF) undergoing cardiac surgery. We performed a single-center data analysis to identify the predictors of rhythm outcome in such patients.

Methods: From January 2003 to January 2012, 503 patients with persistent (n = 296, 58.8%) or paroxysmal (n = 207, 41.2%) AF underwent concomitant surgical AF ablation. The lesions were limited to a pulmonary vein isolation (n = 76, 15.1%), a more complex left atrial lesion set (n = 353, 70.2%), or biatrial lesions (n = 74, 14.7%). Follow-up rhythm evaluations were based on either 24-hour Holter electrocardiograms or event recorder interrogation at 3, 6, and 12 months postoperatively. A sinus rhythm (SR) immediately postoperatively was defined as the first documented rhythm after weaning from extracorporeal circulation.

Results: The mean patient age was 68.0 ± 9.5 years, and 336 (66.8%) were men. No major ablation-related complications occurred. After 1 year of follow-up, 59.9% of all patients were in SR, with significantly better results in patients with paroxysmal AF than in those with persistent AF (67.3% vs 54.8%, $P = .0053$). Additional statistically significant factors influencing SR after 1 year were left atrial diameter ($P = .0019$), AF duration ($P = .018$), and immediate postoperative SR ($P < .001$). Regarding only patients with persistent or longstanding-persistent AF, those with biatrial lesions had significantly greater rates of conversion to SR than those with solitary left atrial ablation (SR, 64.9% vs 51.4%; $P = .044$) after 12 months.

Conclusions: The statistically significant predictors for SR after 1 year were left atrial diameter, AF duration, preoperative paroxysmal AF, immediate postoperative SR, and biatrial ablation for persistent AF. (J Thorac Cardiovasc Surg 2014;148:428-33)

Atrial fibrillation (AF) is the most common sustained arrhythmia in patients undergoing cardiac surgery, and its prevalence has been increasing with the aging of populations. AF can lead to heart failure, thromboembolic events, including stroke, and increased hospitalization, with a reduction in quality of life.[1,2] Therefore, the guidelines have recommended concomitant surgical ablation for patients with AF who are undergoing cardiac surgery.[3] Cox first reported his technique of surgical AF ablation using a cut-and-sew principle in 1987, later revised by him to a lesion pattern termed the "Cox maze III procedure." Because of its high success rate in the restoration of sinus rhythm (SR), it became the reference standard for AF surgery. However, owing to complexity of the procedure, only a few surgeons were performing it.

To facilitate and simplify the procedure, the cut and sew principle was replaced by transmural atrial lesions generated by various thermal energy sources, such as radiofrequency, ultrasonography, or cryotherapy, resulting in the so-called Cox maze IV procedure. Various modified lesion sets, including isolated pulmonary vein ablation, left atrial ablation, and biatrial ablation, have been reported over the years. A meta-analysis by Barnett and Ad[4] showed that in randomized controlled trials and nonrandomized trials, statistically greater rates of conversion to SR occurred in patients who had undergone cardiac surgery with concomitant ablation compared with those who had undergone cardiac surgery alone. Prospective, randomized trials have resulted in rates of conversion to SR of 44% to 94% for patients undergoing concomitant AF ablation.[5-9] However, only a few studies with relatively small numbers of patients have investigated the influence of different lesion sets and energy sources on the outcomes of surgical AF ablation. Therefore, the aim of our study was to analyze the predictors of the 12-month outcome in patients with AF who had undergone concomitant surgical ablation and to determine the effect of different patient factors, energy sources, and lesion sets on the rates of conversion to SR in a large patient cohort with implementation of the current follow-up guidelines.

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Abbreviations and Acronyms

AF = atrial fibrillation
CABG = coronary artery bypass grafting
ECG = electrocardiogram
ER = event recorder
LA = left atrial
LVEF = left ventricular ejection fraction
PVI = pulmonary vein ablation
SR = sinus rhythm

METHODS

Patients

From January 2003 to October 2011, 503 patients underwent concomitant surgical ablation because of persistent (n = 296, 58.8%) or paroxysmal (n = 207, 41.2%) AF. The baseline patient characteristics are listed in Table 1. The mean patient age was 68.0 ± 9.5 years, and 66.8% were men. Of the 503 patients, 296 (58.8%) had preoperative persistent AF and 207 (41.2%) had paroxysmal AF. The mean left atrial (LA) diameter was enlarged to 51.0 mm, and the mean left ventricular ejection fraction (LVEF) showed a normal value of 53.5%. A moderate or more severely reduced LVEF of <40% was present in 61 patients (12.1%). The mean AF duration was 3.4 years, and 51 patients (10.2%) had a experienced a thromboembolic or ischemic stroke before surgery. The surgical procedures are listed in Table 2.

Ablation Methods

The ablation types are listed in Table 3. Isolated pulmonary vein ablation (PVI) was conducted in 76 patients (15.1%). This limited lesion set was used in patients with paroxysmal AF and without planned opening of the atria for the surgical procedure (eg, in patients undergoing coronary artery bypass grafting [CABG] and aortic valve replacement). Extended LA ablation was performed in 353 patients (70.2%) using the LA ablation lesion set of the Cox maze IV procedure, with pulmonary vein ablation, box lesion, LA appendage, and isthmus isolation. Since 2008, biatrial ablation was conducted in 74 patients (14.7%). This extended ablation regimen was only conducted in patients with persistent or longstanding-persistent AF. The decision of which patients underwent a biatrial or LA lesion set was determined by the surgeon performing the procedure. The right atrial lesion set consisted of intercaval line, isolation of the cavotricuspid isthmus, right atrial appendage, and terminal crest.

The energy sources were argon-based cryoablation in 114 patients (22.7%; CryoCath Surgical Ablation Probe, Medtronic, Inc, Minneapolis, Minn; and CryoICE Cryoablation probe, Atricure, Inc, West Chester, Ohio), unipolar radiofrequency ablation in 261 (51.8%; Cardioblate Unipolar RF Pen, Medtronic), and bipolar radiofrequency ablation in 128 (25.5%; Cardioblate BP2 device and Cardioblate Surgical Ablation System Generator, Medtronic; and Atricure Isolater Synergy Ablation Clamp, Atricure). From 2003 to 2009, epimyocardial cryoablation was used in patients receiving surgical AF ablation without opening the left atrium; all other patients received endomyocardial ablation using unipolar radiofrequency. Since 2009, after introduction of the bipolar radiofrequency clamp in our institution, it has become the preferred tool for all strategies of ablation. Since then, endomyocardial unipolar radiofrequency or cryoablation has only been used in patients requiring mitral valve treatment with either an open sternum transseptal or a minimally invasive thoracic-lateral approach.

Statistical Analysis

A retrospective, single-center data analysis was accomplished. All statistical analyses were performed using the Statistical Package for Social Sciences statistical software, version 18.0 (SPSS, Inc, Chicago, Ill). Continuous values are presented as mean ± standard deviation and were compared using the Student *t* test. Categorical variables are presented as the frequencies and percentages and were compared using the chi-square test or Fisher's exact test, as appropriate. $P < .05$ was considered statistically significant. The reported P values are 2-sided. Uni- and multivariate logistic regression analyses were used to identify independent predictors for SR after 12 months. The parameters considered for univariate analysis were age, gender, LA diameter, AF type and duration, LVEF, type of concomitant procedure, lesion set, energy source, and early AF recurrence. For multivariate logistic regression analysis, we included the significant covariates from the univariate analysis and the covariates that in our experience had been considered clinically relevant. These were age, gender, AF type and duration, surgical procedure, LVEF, and LA diameter.

Follow-up Protocol

Rhythm follow-up was accomplished after 3, 6, and 12 months in all patients using either 24-hour Holter electrocardiograms (ECGs) (n = 353) or event recorder (ER) interrogation (n = 149). In patients with ER, AF recurrence was defined as an AF burden > 0.5% and/or a duration of a single AF episode of >30 s. ER-documented AF episodes were manually validated. In patients without ER, a 24-hour Holter ECG was recorded at 3, 6, and 12 months postoperatively. In the latter group, any episode of AF with a duration >30 s was regarded as AF recurrence. Antiarrhythmic drugs and anticoagulation regimens were maintained for 3 months postoperatively in all patients and then adapted according to the ER or 24-hour ECG rhythm results. In patients without a contraindication, amiodarone was used as the first-line antiarrhythmic therapy. Otherwise, other class I or class III antiarrhythmic drugs were prescribed for ≥3 months postoperatively. Antiarrhythmic medical therapy was stopped when the patients were in SR at 3 months of follow-up. Electrical cardioversion was performed in patients with persistent AF at the follow-up examination. Patients with AF recurrence at 6 months postoperatively were considered for additional catheter-based ablation, if reasonable. Patients receiving additional catheter-based ablation were considered to have failure of surgical AF ablation for rhythm analysis after 12 months.

RESULTS

Perioperative Data and Outcomes

No major ablation-related complication occurred in any of the patients. A perforation of the posterior wall of the left atrium was present in 1 patient after cryoablation and was sutured without additional complications. No intraoperative deaths occurred. Five patients (0.9%) experienced perioperative stroke. The in-hospital mortality was 1.2%, and the 1-year survival rate was 94.9%. The stroke-free survival rate after 1 year was 97.2%.

Concomitant procedures and ablation type are listed in Table 2. Most procedures included mitral (n = 151, 30.0%) or aortic valve (n = 53, 10.5%) surgery. CABG was performed in 126 patients (25.1%), tricuspid valve replacement in 8 patients (1.6%), and aortic surgery in 14 patients (2.0%). Combined mitral valve replacement and tricuspid valve replacement was performed in 46 patients (9.2%), mitral valve replacement and aortic valve replacement in 25 (5.0%), and mitral valve replacement plus CABG in 58 (11.5%). Other procedures were conducted in 22 patients (4.4%).

TABLE 1. Patient characteristics (n = 503)

Characteristic	Value
Age (y)	68.0 ± 9.5
Gender	
Female	336
Male	167
AF duration (y)	4.0 ± 3.7
Paroxysmal AF	207 (41.2)
Persistent AF	296 (58.8)
LA diameter (mm)	51.0 ± 8.9
LVEF (%)	52.6 ± 11.0
LVEF < 40%	61 (12.1)
Previous stroke	51 (10.1)
Diabetes	95 (18.9)
Renal insufficiency	55 (10.9)
Preoperative pacemaker use	34 (6.8)
Peripheral arterial disease	29 (5.8)
COPD	51 (10.1)
Coronary artery disease	240 (47.7)
Previous MI	50 (9.9)

Data presented as mean ± standard deviation or n (%). *AF,* Atrial fibrillation; *LA,* left atrial; *LVEF,* left ventricular ejection fraction; *COPD,* chronic obstructive pulmonary disease; *MI,* myocardial infarction.

Rhythm Results

The completeness of follow-up was 96% after 12 months. The overall rate of conversion to SR was 49.8%, 57.6%, and 59.9% after 3, 6, and 12 months, respectively (Figure 1). In patients with preoperative paroxysmal AF, the rate of conversion to SR after 12 months was significantly greater than that in patients with persistent AF (SR, 67.3% vs 54.8%; $P = .0053$). The rate of registered SR did not differ significantly between the ER and Holter-monitored patients after 12 months (63.2% vs 58.5%). Neither demographic data nor the type of concomitant procedure nor pre-existing disease had a significant effect on SR after 1 year (Table 4).

Radiofrequency ablation was used in 389 patients (77.3%), either unipolar (n = 261) or bipolar (n = 128), with a 57.3% conversion rate to SR in the unipolar and 62.7% conversion rate to SR in the bipolar group (Figure 2). Between the 2 groups, no significant differences were found in the preoperative AF type, with 38.2% paroxysmal AF in the unipolar and 44.3% in the bipolar group ($P = .12$). Cryoablation was performed in 114 patients (22.7%), with a 60.7% conversion rate to SR. All together, the type of energy source used did not significantly influence the restored SR rate after 12 months.

Complete left-sided ablation was accomplished in 353 patients (70.2%), and pulmonary vein isolation only was conducted in 76 (15.1%). PVI was only used in patients with paroxysmal AF. In the population with paroxysmal AF, no statistically significant difference was found in the SR rate after 12 months between patients with a complete LA lesion set and those with only PVI (69.3% vs 64.4%, $P = .43$; Figure 3). In the 296 patients with persistent and longstanding-persistent AF, those with biatrial lesion sets had significantly greater rates of SR after 1 year than the LA ablation group (SR, 64.9% vs 51.4%; $P = .044$; Figure 4). Additional predictors for SR after 12 months were the LA diameter and AF duration. Patients with a smaller LA diameter ($P = .0019$) and shorter AF duration ($P = .018$) had significantly greater rates of SR after 1 year. Stratifying the patients into groups with different LA diameters, patients with an LA diameter < 5 cm, 5 to 6 cm, and >6 cm had a sinus rhythm rate of 66.2%, 59.3%, and 44.1%, with a statistically significant lower SR rate in patients with an LA diameter > 6 cm ($P < .001$). SR immediately postoperatively (68.6% SR after 1 year, $P < .001$) was an independent predictor of SR after 1 year.

TABLE 2. Surgical procedures (n = 503)

Procedure	n (%)
CABG	130 (32.4)
AVR	153 (38.2)
MVR	202 (50.4)
TVR	47 (11.7)
MVR plus TVR	50 (9.9)
MVR plus CABG	50 (9.9)
MVR plus AVR	39 (7.8)
Aortic surgery	24 (4.8)

CABG, Coronary artery bypass grafting; *AVR,* aortic valve replacement; *TVR,* tricuspid valve replacement; *MVR,* mitral valve replacement.

TABLE 3. Types of ablation (n = 503)

Ablation type	n (%)
Cryoablation	114 (22.7)
Radiofrequency	389 (77.3)
Unipolar	261 (51.9)
Bipolar	128 (25.4)
LA	353 (70.2)
Biatrial	74 (14.7)
PVI	76 (15.1)

LA, Left atrial; *PVI,* pulmonary vein ablation.

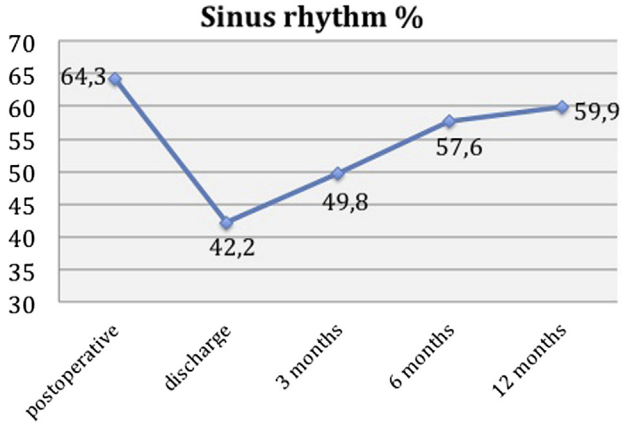

FIGURE 1. Sinus rhythm rate during follow-up.

TABLE 4. Influence of patient factors and procedures on sinus rhythm rate after 12 months by multivariate logistic regression analysis

Variable	*P* value
Age (y)	.723
Male gender	.179
Paroxysmal AF	.005*
LA diameter	.002*
AF duration	.019*
Coronary artery disease	.155
Preoperative LVEF	.256
CABG	.058
AVR	.266
MVR	.096
Cryoablation	.837
Radiofrequency unipolar	.218
Radiofrequency bipolar	.277
LA lesion set	.308
PVI	.859
Biatrial lesion set	.343
Immediate postoperative SR	<.001*

AF, Atrial fibrillation; *LA*, left atrial; *LVEF*, left ventricular ejection fraction; *CABG*, coronary artery bypass grafting; *AVR*, aortic valve replacement; *MVR*, mitral valve replacement; *PVI*, pulmonary vein ablation; *SR*, sinus rhythm. *Paroxysmal AF, .0053; LA diameter, .0019; AF duration, .018; immediate postoperative SR, .001.

Additional catheter-based ablation was performed in 26 patients (5.2%), and electrical cardioversion was conducted in 54 patients (10.7%) within 1 year of follow-up.

DISCUSSION

The original Cox maze procedure, first reported by Cox in 1987, was revised to the Cox maze III procedure, which became the reference standard for AF ablation. In many comparisons, the Cox maze III procedure has been reported to be the most effective therapy for AF, resulting in success rates of ≤99%.[10,11] Replacing the original cut and sew principles by ablation with different energy sources to create transmural thermal atrial lesions led to the Cox maze IV procedure. This modified Cox maze procedure has been shown to be as effective as the classic cut and sew maze technique. Lall and colleagues[12] showed similar results in a propensity score-matched analysis for patients undergoing the Cox maze III and IV procedures, with a success rate of 96% and 93%, respectively, after 1 year of follow-up. Surgical AF ablation can be conducted either as a standalone or concomitant procedure. In the present study, we have reported our experience with surgical AF ablation as a concomitant procedure.

To date, 6 prospective randomized trials have reported the results of concomitant surgical ablation for patients with AF. The largest trial included 97 patients with

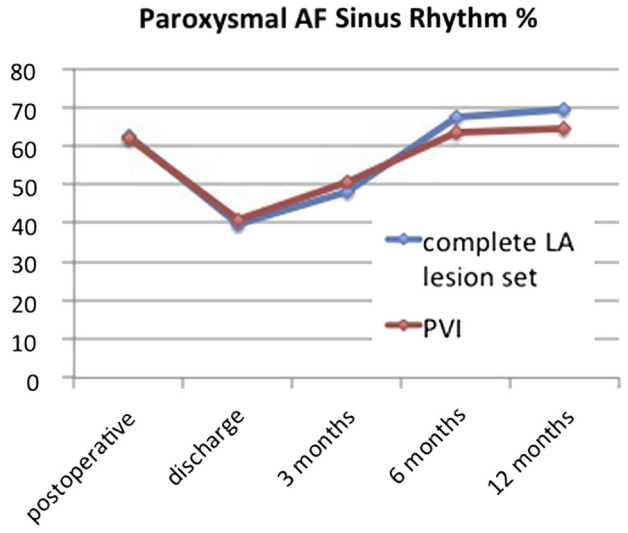

FIGURE 3. Sinus rhythm rate during follow-up in patients with paroxysmal atrial fibrillation (*AF*). *LA*, Left atrial; *PVI*, pulmonary vein ablation.

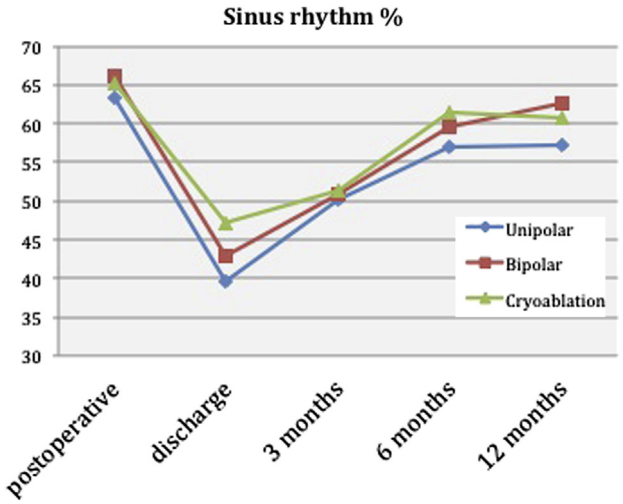

FIGURE 2. Sinus rhythm rate stratified by different energy sources.

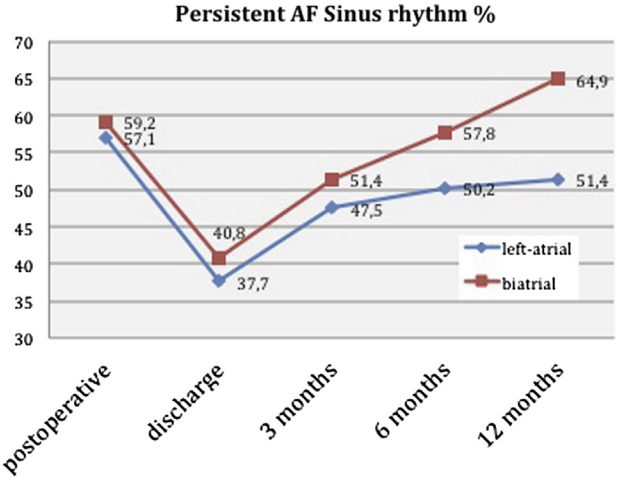

FIGURE 4. Sinus rhythm rate during follow-up in patients with persistent atrial fibrillation (*AF*).

persistent AF who were referred for mitral valve surgery. The patients were randomized to either mitral valve surgery and LA radiofrequency ablation or mitral valve surgery only. Patients with concomitant ablation showed significantly greater rates of SR after 1 year (44% vs 4.5%).[9] This finding was replicated in other prospective randomized trials.[5-8] The rates of SR ranged from 57% to 82% in these studies. However, because of the small number of patients and the resulting limited statistical power, none of the randomized trials was able to show a survival benefit for patients receiving concomitant ablation. However, in a recent propensity score-matched analysis by McCarthy and colleagues,[13] the midterm survival of patients with AF receiving concomitant surgical ablation was significantly greater statistically compared with the untreated patients and comparable to those of patients without preoperative AF.

Great variability was also found in the ablation success rates in recent retrospective studies, with SR rates ranging from 67% to 84% in patients with AF undergoing concomitant surgical ablation.[14-20] These variations were most likely the result of the use of different lesion sets, energy sources, surgeon experience, and implemented follow-up strategies, which varied from symptom-oriented patient interviews to continuous rhythm monitoring.

Our retrospective data series contained a large number of patients treated during a long period and using different line sets and energy sources for AF ablation. We found that the energy source type used for ablation did not have any effect on SR after 12 months, which has also been seen in previously published studies.[20,21] However, a few reports, although none prospective, have been published reporting that the success of ablation depended on energy source used.

Regarding the different lesion sets, a study by Gillinov and colleagues[14] and a meta-analysis by Barnett and Ad[4] have shown biatrial lesion sets to be superior to LA lesion sets in patients with persistent AF. This finding was supported in our series in the multivariate analysis when assessing only patients with persistent AF. A significantly greater SR rate was seen in patients with biatrial lesion sets than in those receiving only LA ablation. However, a greater incidence of postoperative permanent pacemaker implantation was observed in patients receiving a biatrial lesion set in a study by Worku and colleagues[22] and in our previously published data.[23]

The present study is 1 of the first series to implement the recent guidelines for follow-up.[3] All rhythm results were collected using either 24-hour Holter ECG or ER interrogation. All patients had $\geq$1 24-hour Holter ECG or ER interrogation at 3 and 12 months of follow-up. Especially in patients with paroxysmal AF, this allowed a more accurate analysis of the actual rhythm and ablation success rates. Previous studies have shown that short-term rhythm monitoring underestimates the rate of AF recurrence after ablation therapy,[24,25] and the more extended follow-up period might have been the reason for the lower SR rates compared with the previously published results of surgical AF ablation with less extensive follow-up strategies. Gillinov and colleagues[14] reported in a retrospective study a rate of SR of 76% at 1 year after surgical AF ablation in patients with persistent AF. However, the rhythm results were based only on the ECG findings, and the conversion rate might have been lower if the results had included repeated 24-hour Holter ECG or continuous rhythm monitoring using ER.

On multivariate analysis, no association was found between gender, age, coronary artery disease, LVEF, and the type of concomitant procedure and the rates of SR after 1 year. In previously published studies,[14,17] older age resulted in a greater rate of AF recurrence; however, we could not confirm this finding in our study.

In the present study, a LA diameter $>$ 6 cm was an independent predictor for successful ablation. Similar observations were reported by Damiano and colleagues[15] and Gillinov et al.[18,19] The AF duration was also an independent predictor of greater rates of SR after 1 year. This result was supported in a previous study by Gaynor and colleagues[16] but could not be confirmed in their more recent analysis for predictors of late recurrence in Cox maze IV procedures.

Immediate postoperative SR was an independent predictor of ablation success after 12 months. Similar results have been published by Damiano and colleagues.[15] They found that patients with early recurrence of atrial tachycardias also had greater rates of AF recurrence after 1 year.[15] All our patients received amiodarone for 3 months postoperatively. It remains unknown whether a more extensive cardioversion regimen with additional electrical cardioversion in patients with early recurrence of atrial tachycardia would have improved the long-term outcomes, although it is probable that early recurrence of atrial tachycardia is also evidence for the presence of an additional pathologic atrial substrate that maintains these arrhythmias. Additional investigation is needed to address this question.

Our success rates were significantly greater in patients with preoperative paroxysmal AF than in those with persistent AF, just as previously published,[14,18,19] and was not surprising. In patients with paroxysmal AF, reentry circuits play a major role, and a pathologic substrate available to sustain atrial tachyarrhythmias is likely less.[26]

A major limitation of the present study was that we used a nonrandomized retrospective study design, in which unknown confounders and selection and detection bias could not be completely avoided. Furthermore, the present study was a single-center analysis.

Concomitant surgical ablation for AF showed a SR conversion rate of 59.9% after 1 year of follow-up. The statistically significant predictors for SR after 1 year were preoperative paroxysmal AF, LA diameter, AF duration, and SR immediately postoperatively. In patients with persistent AF, those receiving a biatrial lesion set showed a statistically significant greater SR conversion rate after 12 months of follow-up. However, different energy sources and the type of concomitant procedure did not influence the SR rate.

Because of previously published data and our own experience, our current ablation strategy includes a biatrial lesion set in patients with persistent AF. In most patients with paroxysmal AF, a complete LA lesion set is performed, and only PVI is performed in patients undergoing off-pump CABG and some of the patients undergoing aortic valve replacement or CABG without opening the left atrium.

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